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ISCHAEMIC HEART DISEASE

There is no need to ''cool-off'' the ACS before intervention ► Once the benefits of percutaneous coronary intervention (PCI) in acute coronary syndromes had been accepted, the next decision was on whether to do it very early, or after a cooling-off period of 2–3 days. This period would allow some settling of inflammatory and thrombotic tendency with appropriate medical treatment, making PCI safer. Not so it seems. Patients were randomly allocated to antithrombotic pretreatment for 3–5 days or to early intervention after pretreatment for less than six hours. In both groups, antithrombotic pretreatment consisted of intravenous unfractionated heparin, aspirin, clopidogrel (600 mg loading dose followed by 75 mg twice daily dose), and intravenous tirofiban. The primary end point was reached in 11.6% (three deaths, 21 infarctions) of the group receiving prolonged antithrombotic pretreatment and in 5.9% (no deaths, 12 infarctions) of the group receiving early intervention (relative risk (RR) 1.96, 95% confidence interval (CI) 1.01 to 3.82; p = 0.04). This outcome was attributable to events occurring before catheterisation; after catheterisation, both groups incurred 11 events each (p = 0.92).

▲ **Neumann F-J**, Kastrati A, Pogatsa-Murray G, Mehilli J, Bollwein H, Bestehorn H-P, Schmitt C, Seyfarth M, Dirschinger J, Schömig A. Evaluation of prolonged antithrombotic pretreatment (''cooling-off'' strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. *JAMA* 2003;**290**:1593–9

Cypher stents reduce restenosis rates to 5.9% even in small arteries ► Small arteries restenose aggressively after stenting. Drug eluting stents offer a possible solution. The mean diameter of treated coronary arteries was 2.55 mm and mean lesion length was 15.0 mm. Multiple stents were implanted in 170 (48%) patients. At eight months, minimum lumen diameter was significantly higher with sirolimus eluting stents than with control stents (2.22 mm *v* 1.33 mm, $p < 0.0001$). The rate of binary restenosis was significantly reduced with sirolimus eluting stents compared with control stents (5.9% *v* 42.3%, p = 0.0001). These stents were implanted in a ''real world'' fashion, with no routine predilatation or intravascular ultrasound, making the data all the more startling. In the US branch of the trial results were similar, but the diabetic subgroup showed that the battle over restenosis has not been won (restenosis rates in drug eluting stent versus normal stent: 17.6% *v* 50.5%, $p < 0.001$). National Institute for Clinical Excellence guidelines have just been produced recommending use of these stents in vessels < 3 mm diameter and lesions > 20 mm long.

▲ **Schofer J**, Schlüter M, Gershlick AH, Wijns W, Garcia E, Schampaert E, Breithardt G, for the E-SIRIUS Investigators. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS) *Lancet* 2003;**362**:1093–9.

▲ **Moses JW**, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, Caputo RP, Kereiakes DJ, Williams DO, Teirstein PS, Jaeger JL, Kuntz RE, for the SIRIUS Investigators. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003; **349**:1315–23.

Presence of thrombus predicts worse outcome after primary angioplasty ► Most people agree that primary PCI is better than thrombolysis for acute myocardial infarction (MI). However, a suboptimal result after PCI, even with an open artery, is a marker of bad outcome—presumably because of distal embolisation of thrombus. Tirofiban administered before primary PCI might reduce this risk. This study suggests that if the vessel is still occluded, or there is thrombus seen proximal to the lesion at angiography, then outcomes are poor even if glycoprotein IIb/IIIa blockers have been used. Distal protection devices or thrombus extraction might have helped, but were not used.

▲ **Yip H-K**, Wu C-J, Chang H-W, Hsieh Y-K, Fang C-Y, Chen S-M, Chen M-C. Impact of tirofiban on angiographic morphologic features of high-burden thrombus formation during direct percutaneous coronary intervention and short-term outcomes. *Chest* 2003;**124**:962–8.

Good evidence for aspirin as primary prevention ► In 1988, the aspirin component of the physicians' health study, a randomised, double blind, placebo controlled trial of 22 071 apparently healthy men, was terminated early due to a 44% ($p < 0.00001$) reduction in the risk of a first MI. The British doctors' trial of 5139 men showed no significant benefits. Since that time, three additional randomised trials have been published: the thrombosis prevention trial (5085), the hypertension optimal treatment study (18 790), and the primary prevention project (4495). Among the 55 580 randomised participants (11 466 women), aspirin was associated with a significant 32% reduction in the risk of a first MI and a significant 15% reduction in the risk of all important vascular events, but had no significant effects on non-fatal stroke or vascular death. No harm was done in any study despite the worries about bleeding. The benefits of aspirin in preventing colon cancer are an additional benefit.

▲ **Eidelman RS**, Hebert PR, Weisman SM, Hennekens CH. An update on aspirin in the primary prevention of cardiovascular disease *Arch Intern Med* 2003;**163**:2006–10.

The final nail in the coffin of antibiotics for treatment of coronary heart disease? ► Stable patients with previous acute MI received either azithromycin (600 mg/day for three days during week 1, then 600 mg/week during weeks 2–12; n = 3879) or placebo (n = 3868). After a median of 14 months of follow up, there was no significant risk reduction in the likelihood of a primary event (death/MI/PCI/admission with angina) with azithromycin versus placebo (7%, 95% CI −5% to 17%; p = 0.23). Subgroup analysis suggested possible early benefits of azithromycin on death/reinfarction, but these decreased over time. Although it is possible that longer term treatment might be of benefit, this has not been proven.

▲ **O'Connor CM**, Dunne MW, Pfeffer MA, Muhlestein JB, Yao L, Gupta S, Benner RJ, Fisher MR, Cook TD, for the Investigators in the WIZARD Study. Azithromycin for the secondary prevention of coronary heart disease events: the WIZARD study: a randomized controlled trial. *JAMA* 2003;**290**:1459–66.

HEART FAILURE

Heart failure occurs earlier in UK Asians than whites, but prognosis is not worse ► People of South Asian origin (Indian subcontinent) comprise the largest ethnic minority group in the UK—4.1% of the population in 2001. When compared with the white population, South Asian patients had significantly higher age adjusted admission rates (rate ratio 3.8 for men and 5.2 for women) and hospital incidence rates (2.2 and 2.9). Among 5789 incident cases of heart failure, South Asian patients were younger and more often male than white patients (mean (SD) 70 (0.6) *v* 78 (0.1) years and 56.5% (190/336) *v* 49.3% (2494/5057), respectively). South Asian patients were also more likely to have previous acute MI (10.1% (n = 34) *v* 5.5% (n = 278)) or concomitant acute MI (18.8% (n = 63) *v* 10.7% (n = 539)) or diabetes (45.8% (n = 154) *v* 16.2% (n = 817), all $p < 0.001$). However, South Asian patients had a significantly lower risk of death (hazard ratio (HR) 0.82, 95% CI 0.68 to 0.99) and a similar probability of death or readmission (HR 0.96, 95% CI 0.81 to 1.09) compared with white patients.

▲ **Blackledge HM**, Newton J, Squire IB. Prognosis for South Asian and white patients newly admitted to hospital with heart failure in the United Kingdom: historical cohort study. *BMJ* 2003;**327**:526–31.

HYPERTENSION

Thiazides may reduce hip fractures in elderly HT patients ► Which antihypertensive agent should we use? In diabetes and renal disease, angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers are gaining ground. However, the ALLHAT trial suggests that older agents still have a place. In patients > 75 years, relative to non-use, current use of thiazides for more than 365 days was significantly associated with a lower risk for hip fracture (HR 0.46, 95% CI 0.21 to 0.96). There was no clear dose dependency. This lower risk disappeared approximately four months after thiazide use was discontinued. Thiazides are thought to protect against age related bone loss by reducing urinary calcium excretion.

▲ **ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group**. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). *JAMA* 2003;**288**:2981–97.

▲ **Schoofs MW**, van der Klift M, Hofman A, de Laet CE, Herings RM, Stijnen T, Pols HA, Stricker BH. Thiazide diuretics and the risk for hip fracture. *Ann Intern Med* 2003;**139**:476–82.

GENERAL CARDIOLOGY

What to expect from tilt testing ► Patients underwent a 70° upright tilt for 40 minutes, followed by a 20 minute tilt while receiving isoproterenol hydrochloride. The results of tilt table tests were considered positive when clinical symptoms were reproduced in association with a decline in blood pressure. Of 694 tests, 222 were positive. Eighteen patients (8%) had apparent neurologic events during tilt table testing, including 11 patients (5%) with apparent tonic–clonic seizure-like activity. These patients had lower blood pressure and heart rate during the test than the rest. Perhaps the neurologists should order more tilt tests?

▲ **Passman R**, Horvath G, Thomas J, Kruse J, Shah A, Goldberger J, Kadish A. Clinical spectrum and prevalence of neurologic events provoked by tilt table testing. *Arch Intern Med* 2003;**163**:1945–8.

What is the value of the treadmill test in asymptomatic women? ► In a sample of 2994 asymptomatic women, there were 427 (14%) deaths during 20 years of follow up, of which 147 were due to cardiovascular causes. Low exercise capacity, low heart rate recovery (HRR), and not achieving target heart rate were independently associated with increased all cause and cardiovascular mortality. There was no increased cardiovascular death risk for exercise induced ST segment depression (age adjusted hazard ratio 1.02, 95% CI 0.57 to 1.80; p = 0.96). The age adjusted hazard ratio for cardiovascular death for every metabolic equivalent (MET) decrement in exercise capacity was 1.20 (95% CI 1.18 to 1.30; p < 0.001); for every 10 beats per minute decrement in HRR, the hazard ratio was 1.36 (95% CI 1.19 to 1.55; p < 0.001). Among women with low risk Framingham scores, those with below median levels of both exercise capacity and HRR had significantly increased risk compared with women who had above median levels of these two exercise variables, 44.5 and 3.5 cardiovascular deaths per 10 000 person-years, respectively (hazard ratio for cardiovascular death 12.93, 95% CI 5.62 to 29.73; p < 0.001).

▲ **Mora S**, Redberg RF, Cui Y, Whiteman MK, Flaws JA, Sharrett AR, Blumenthal RS. Ability of exercise testing to predict cardiovascular and all-cause death in asymptomatic women: a 20-year follow-up of the lipid research clinics prevalence study. *JAMA* 2003;**290**:1600–7.

Diet and exercise improve insulin resistance in syndrome X ► Reavens syndrome has a constellation of cardiovascular risk factors. A total of 53 men and women were selected from a larger behavioural intervention trial, who showed the hyperinsulinaemia, dyslipidaemia, and high blood pressure characteristic of syndrome X. Participants were randomly assigned to exercise (EX) only (n = 21), EX + weight loss (WL) (n = 21), or a waiting list control group (n = 11). Before and following treatment, participants underwent measurement of glucose tolerance, lipid values, and clinical blood pressure. Although there was no improvement in lipids, diastolic blood pressure was reduced in the combined therapy group (mean (SD) 96 (4) to 87 (5) mm Hg; p = 0.01), but not in the EX only group (93 (4) to 89 (5) mm Hg; p = 0.08). Insulin resistance improved in all treatment groups compared to controls, and related to weight loss.

▲ **Watkins LL**, Sherwood A, Feinglos M, Hinderliter A, Babyak M, Gullette E, Waugh R, Blumenthal JA. Effects of exercise and weight loss on cardiac risk factors associated with syndrome X. *Arch Intern Med* 2003;**163**:1889–95.

Convincing patients of the benefits of warfarin in AF ► A large amount of data suggests that warfarin therapy reduces stroke risk in atrial fibrillation (AF). This study suggests that even if stroke occurs, outcome is better if the patient was on warfarin. Ischaemic stroke was studied in a cohort of 13 559 patients with non-valvar AF. Strokes were identified through hospitalisation databases and validated on the basis of medical records, which also provided information on the use of warfarin or aspirin, the international normalised ratio (INR) at admission, and coexisting illnesses. Of 596 ischaemic strokes, 32% occurred during warfarin therapy, 27% during aspirin therapy, and 42% during neither type of therapy. Among patients who were taking warfarin, an INR < 2.0 at admission, as compared with an INR ⩾ 2.0, independently increased the odds of a severe stroke (hazard ratio for death within 30 days 3.4, 95% CI 1.1 to 10.1). An INR of 1.5–1.9 at admission was associated with a mortality rate similar to that for an INR < 1.5 (18% and 15%, respectively). The 30 day mortality rate among patients who were taking aspirin at the time of the stroke was similar to that among patients who were taking warfarin and who had an INR < 2.0.

▲ **Hylek EM**, Go AS, Chang Y, Jensvold NG, Henault LE, Selby JV, Singer DE. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. *N Engl J Med* 2003;**349**:1019–26.

Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

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